



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,417	01/17/2002	David Harrow Gelfand	1803-0329-999	4095

41504 7590 08/22/2005

TOWNSEND AND TOWNSEND AND CREW, LLP
2 EMBARCADERO CENTER, 8TH FLOOR
SAN FRANCISCO, CA 94111

EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
----------	--------------

1634

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/052,417	Applicant(s) GELFAND ET AL.	
	Examiner Jehanne S. Sitton	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-8, 10-13, 16-18, 20-23, 26, 27, 29, 31-37, 39-43, 45-48 and 50-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 10, 11, 20-23, 29, 31-34, 37, 39-43, 45, 47, 48, 50 and 53 is/are rejected.
- 7) ☒ Claim(s) 2, 3, 6-8, 11-13, 16-18, 26, 27, 35, 36, 43, 46, and 51-53 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>3</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

HL

DETAILED ACTION

1. Currently, claims 1-3, 6-8, 10-13, 16-18, 20-23, 26-27, 29, 31-37, 39-43, 45-48, and 50-53 are pending in the instant application. The following rejections constitute the complete set being presently applied to the instantly pending claims. Response to arguments, follow, where appropriate. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection under 35 USC 112/2nd paragraph made at section 5 of the previous office action is withdrawn in view of the amendments to the claims.

4. The rejections made under 35 USC 102 and 103 at sections 9-13 of the previous office action are withdrawn in view of the amendments to the claims to define position 6 of SEQ ID NO: 1 as either Ala or Ser, however the rejection under 35 USC 103 is maintained with regard to claim 53.

Claim Objections

5. Claim 11 is objected to because of the following informalities: Claim 11, recites “the amino acids sequence” twice in part (i) of b. Appropriate correction is required.

6. Claims 12, 43, and 53 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

Art Unit: 1634

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

7. Claims 2, 3, 6-8, 13, 16-18, 26, 27, 35, 36, 46, and 51- 52 are objected to for being dependent on rejected claims.

Maintained Rejections

Claim Rejections - 35 USC § 112

8. Amended claims 1, 10, 11, 20-23, 29, 31-34, 37, 39, 43, 45, 47, 48, 50 and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant thermostable DNA polymerase comprising SEQ ID NO: 1 whereby XAA at positions 3, 9, and 10 are any amino acid residue, XAA at position 6 is Ala or Ser, XAA at position 7 is Ile and XAA at position 4 is not Glu, and said thermostable DNA polymerase has a level of discrimination against incorporation of nucleotides labeled with fluorescein family dyes which is reduced in comparison to a polymerase whose sequence is identical to that of said thermostable DNA polymerase except that XAA at position 4 is Glu, a nucleic acid encoding said recombinant thermostable polymerase, as well as methods of using and kits containing said recombinant thermostable polymerase, does not reasonably provide enablement for the instantly amended claims directed to recombinant thermostable DNA polymerase comprising SEQ ID NO: 4 whereby XAA at position 7 is Val or Ile and XAA at position 4 is not Arg, and said thermostable DNA polymerase has a level of discrimination against incorporation of nucleotides labeled with fluorescein family dyes which is reduced in comparison to a polymerase whose sequence is identical to that of said thermostable DNA polymerase except that XAA at position 4

Art Unit: 1634

is Arg, a nucleic acid encoding said recombinant thermostable polymerase, as well as methods of using and kits containing said recombinant thermostable polymerase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The claims are drawn to thermostable DNA polymerases which comprise SEQ ID NO: 4 whereby XAA at position 7 is Val or Ile and XAA at position 4 is not Arg, and said thermostable DNA polymerase has a level of discrimination against incorporation of nucleotides labeled with fluorescein family dyes which is reduced in comparison to a polymerase whose sequence is identical to that of said thermostable DNA polymerase except that XAA at position 4 is Arg, a nucleic acid encoding said recombinant thermostable polymerase, as well as methods of using and kits containing said recombinant thermostable polymerases.

The specification teaches that the use of fluorescent dyes is important for many in vitro DNA applications. The specification teaches producing template dependent thermostable DNA polymerase enzymes having reduced discrimination against incorporation of nucleotides labeled

Art Unit: 1634

with fluorescein family dyes (see p. 2, lines 22-25). The specification teaches that a recombinant Taq DNA polymerase enzyme which contained two mutations was constructed. The first was an E to K mutation at position 4 of the critical motif of the invention (see p. 4, lines 24-26). The specification teaches that this mutation identified a region in the DNA polymerase gene that affects the ability of the polymerase to interact with negatively charged fluorescent nucleotides. The specification teaches that this site, distal to helix O is at the end of the Oa helix and the beginning of the Ob helix of the polymerase (see p. 12, lines 24-28). The specification teaches that based on molecular modeling principles, changes in the structure of the Oa-Ob helix other than E (Glu) to K (Lys) are also expected to produce changes in the ability of the polymerase to discriminate against nucleotides labeled with fluorescein family dyes. The specification provides no evidence or working examples of a thermostable polymerase comprising SEQ ID NO: 4, where Xaa at position 7 is Val or Ile, and Xaa at position 4 is any amino acid residue other than Arg, wherein the polymerase has a level of discrimination against the incorporation of fluorescein family dyes which is reduced in comparison to a polymerase as noted above with an Arg at position 4). In response to rejections under 112/1st paragraph made in parent application 09/146,631, a declaration under 35 USC 1.132 was submitted by Dr. Gelfand for the instantly pending application. The declaration showed that for Tth polymerase, when position 4 of SEQ ID NO: 1 was mutated to any of the 19 amino acids other than Glu, the polymerase showed reduced discrimination against the incorporation of nucleotides labeled with HEX-2-PA, a fluorescein family dye analog. However, the declaration shows that Arginine showed the most reduced level of discrimination (see Figure 1 of declaration of 1/3/2003). Accordingly, it is clear that if in fact, position 4 of SEQ ID NO: 1 is the "critical" position with regard to the

Art Unit: 1634

discrimination of incorporation of nucleotides labeled with fluorescein family dyes as asserted in the specification and declaration, the claims specifically recite polymerases, where if position 4 was mutated in comparison to an amino acid other than Arg (for example, found at position 4 of the critical motif in *Thermotoga maritima*, *Thermatoga neopolitana*, and *Thermosifo africanus*; page 15 of specification), such polymerases would in fact not be predictably expected to have reduced discrimination against the incorporation of fluorescein family dyes as compared to a polymerase comprising SEQ ID NO: 4 with Arg at position 4. The claims specifically recite embodiments (polymerases from *Thermosifo africanus* as well as polymerases from *Thermatoga*) where no mutation at position 4 would be predictably expected to produce a mutant polymerase with the function recited in the claims given the results shown in the declaration.

While the claimed invention encompass polymerases comprising SEQ ID NO: 1, 2, 3, or 4, and such SEQ ID NOS: contain additional undefined amino acid positions, the specification has not provided any teaching or guidance as to any mutation at such positions which would lead to a mutant polymerase with reduced discrimination against the incorporation of nucleotides labeled with fluorescein family dyes. While molecular modeling techniques exist, such techniques would not be expected to predict which other mutation in any of SEQ ID NO: 1-4 would result in a mutant polymerase with reduced discrimination against the incorporation of nucleotides labeled with fluorescein family dyes. The state of the art with regard to molecular modeling is unpredictable, as evidenced by the teachings of Lomize (Lomize et al, Proteins: Structure, Function and Genetics, suppl. 3, pp 199-203, 1999 : A Prediction of Protein Structure: The Problem of Fold Multiplicity"). Such modeling requires the incorporation of many different parameters, including but not limited to burial of non polar side chains, saturation of hydrogen

Art Unit: 1634

bonding potential, and stereochemical quality. Lomize teaches that many different structures are possible that can simultaneously satisfy these criteria and therefore additional energy contributions must be taken into account (p. 199; col 2). Lomize teaches attempting to model four CASP3 target, using simple modeling procedure (see abstract). Lomize teaches that although this approach allows construction of 3D models that in some cases properly reproduce the structural class of the protein the four models predicted were incorrect (see abstract, and p. 200, col 2). Lomize teaches that such results indicate that hydrophobicity patterns do not unequivocally determine protein folds. Thus from the teaching of Lomize, the skilled artisan would have recognized that molecular modeling is not yet a precise science, and that relying on such to predict the function of a particular residue is unpredictable, especially given that the specification does not teach how the residue functions to achieve the desired result or the specific programs, algorithms and parameters that the skilled artisan would use (as Lomize teaches that such are important in predicting structure or function) to determine which residues would give the desired results. Further, as shown by declaration of 1/3/2003 at figure 1, the effect of each specific amino acid change is unpredictable with regard to level of reduction in discrimination. Therefore, based on the lack of guidance in the specification, the conflicting evidence of the declaration submitted 1/3/2003, and the unpredictability taught in the art, it would require undue experimentation for the skilled artisan to practice the invention commensurate in scope with the claims. In the instant application, the claims specifically recite embodiments which would not be predictably expected to yield mutant polymerases with the claimed function. Neither the specification nor the art provide any guidance as to which polymerases or what structures would fall within the scope of the claims (ie, mutation at positions in the recited SEQ ID NOS other

Art Unit: 1634

than position 4), especially with regard to polymerases from *Thermosipho africanus*, and *Thermatoga*.

Written Description

9. Amended claims 1, 10, 11, 20-23, 29, 31-34, 37, 39, 43, 45, 47, 48, 50 and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to thermostable DNA polymerases which comprise SEQ ID NO: 4 whereby XAA at position 7 is Val or Ile and XAA at position 4 is not Arg, and said thermostable DNA polymerase has a level of discrimination against incorporation of nucleotides labeled with fluorescein family dyes which is reduced in comparison to a polymerase whose sequence is identical to that of said thermostable DNA polymerase except that XAA at position 4 is Arg, a nucleic acid encoding said recombinant thermostable polymerase, as well as methods of using and kits containing said recombinant thermostable polymerases.

The specification teaches that the use of fluorescent dyes is important for many in vitro DNA applications. The specification teaches producing template dependent thermostable DNA polymerase enzymes having reduced discrimination against incorporation of nucleotides labeled with fluorescein family dyes (see p. 2, lines 22-25). The specification teaches that a recombinant Taq DNA polymerase enzyme which contained two mutations was constructed. The first was an E to K mutation at position 4 of the critical motif of the invention (see p. 4, lines 24-26). The specification teaches that this mutation identified a region in the DNA polymerase gene that

Art Unit: 1634

affects the ability of the polymerase to interact with negatively charged fluorescent nucleotides. The specification teaches that this site, distal to helix O is at the end of the Oa helix and the beginning of the Ob helix of the polymerase (see p. 12, lines 24-28). The specification teaches that based on molecular modeling principles, changes in the structure of the Oa-Ob helix other than E (Glu) to K (Lys) are also expected to produce changes in the ability of the polymerase to discriminate against nucleotides labeled with fluorescein family dyes. The specification does not provide evidence of any thermostable polymerase comprising SEQ ID NO: 4, where Xaa at position 7 is Val or Ile, and Xaa at position 4 is any amino acid residue other than Arg, wherein the polymerase has a level of discrimination against the incorporation of fluorescein family dyes which is reduced in comparison to a polymerase as noted above with an Arg at position 4). In response to rejections under 112/1st paragraph made in parent application 09/146,631, a declaration under 35 USC 1.132 was submitted by Dr. Gelfand for the instantly pending application. The declaration showed that for Tth polymerase, when position 4 of SEQ ID NO: 1 was mutated to any of the 19 amino acids other than Glu, the polymerase showed reduced discrimination against the incorporation of nucleotides labeled with HEX-2-PA, a fluorescein family dye analog. However, the declaration shows that Arginine showed the most reduced level of discrimination (see Figure 1 of declaration of 1/3/2003). Accordingly, it is clear that if in fact, position 4 of SEQ ID NO: 1 is the "critical" position with regard to the discrimination of incorporation of nucleotides labeled with fluorescein family dyes as asserted in the specification and declaration, the claims specifically recite polymerases, where if position 4 was mutated in comparison to an amino acid other than Arg (for example, found at position 4 of the critical motif in *Thermotoga maritima*, *Thermatoga neopolitana*, and *Thermosifo africanus*; page 15 of

Art Unit: 1634

specification), such polymerases would in fact not be predictably expected to have reduced discrimination against the incorporation of fluorescein family dyes as compared to a polymerase comprising SEQ ID NO: 4 with Arg at position 4. The claims specifically recite embodiments (polymerases from *Thermosifon africanus* as well as polymerases from *Thermatoga*) where no mutation at position 4 would be predictably expected to produce a mutant polymerase with the function recited in the claims given the results shown in the declaration.

While the claimed invention encompasses polymerases comprising SEQ ID NO: 1, 2, 3, or 4, and such SEQ ID NOS: contain additional undefined amino acid positions, the specification has not provided any teaching or guidance as to any mutation at such positions which would lead to a mutant polymerase with reduced discrimination against the incorporation of nucleotides labeled with fluorescein family dyes, as recited in the claims.

The claims encompass a large genus of polymerases that have not been taught or described by the specification. The mutant polymerase taught by the specification is not representative of this large genus. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.). The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides or proteins, regardless of the complexity or simplicity of the method of isolation. "Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The

Art Unit: 1634

nucleic acid itself is required." See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

Response to Arguments

The response asserts that in view of the interview, it was Applicant's understanding that the amended claims fulfilled the enablement and written description requirement. This was not found persuasive as the examiner did not indicate that claims directed to the rejected subject matter above, would fulfill either requirement under 112/first para. The claims have been amended to specifically recite embodiments that the previous office action indicated were not allowable under 112/first paragraph.

Claim Rejections - 35 USC § 103

Art Unit: 1634

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hughes in view of Wiemann (Wiemann et al; Analytical Biochemistry, vol. 234, pages 166-174, 1996).

It is noted that instant claim 53 is dependent from claim 50. While it does not further limit the polymerases as set forth in claim 50, claim 53 has been broadly interpreted to encompass a kit containing the polymerase as claimed in claim 53 as well as a ribonucleotide labeled with a fluorescein family dye.

Hughes teaches a mutant recombinant DNA polymerase (SEQ ID NO: 3 of Hughes) from *Thermatoga* (Tne) which is encoded by a nucleic acid sequence (SEQ ID NO: 2 of Hughes), wherein the polymerase comprises the sequence LeuSerValArgLeuGlyIleProValLysGlu

Art Unit: 1634

(residues 741-751). The residue at position "4" is Arg (not mutated to Glu) and the residue at position "7" is Ile, thus meeting the limitations of claim 53. Additionally, Hughes teaches that Tne mutants provide for good incorporation of dye terminators, such dye terminators can be reduced 500 fold (see col. 18, lines 25-30). Further, Hughes teaches packaging the polymerases in kit format (see cols 16 and 17), along with detectably labeled nucleotides, including dye terminators, which can be labeled with fluorescent dyes and which also include rNTP (see col. 8, lines 26-41). Further, Hughes teaches that the Tne polymerase can be used in methods of fluorescent sequencing, which inherently produces labeled DNA and labeled primer extension products. With regard to claim 53 (as being dependent from claim 50), Hughes does not specifically teach the use of or packaging of nucleotides labeled with a negatively charged fluorescent dye or a fluorescein family dye, however Wiemann specifically teaches an improved method of fluorescent DNA sequencing which uses a nucleotide (specifically a dye terminator) which is labeled with fluorescein, which is a negatively charged fluorescent dye (see page 167). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the improved method of fluorescent DNA sequencing in the method of sequencing of Hughes because Wiemann teaches that this technique allows one to obtain simultaneously two independent sequences from one sequencing reaction (see page 166, abstract). It would have been further obvious to one of ordinary skill in the art to include such in the packaged nucleotides of Hughes in order to make the method of Hughes in view of Wiemann easier and more convenient to perform.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 40-43 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 lacks antecedent basis for the recitation of “said thermostable DNA polymerase” because it is unclear which thermostable DNA polymerase the comparison is being made to.

Claim 47 lacks antecedent basis for the recitation of “the XAA at position 4” because it is unclear which position “4” is being referred to.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1634

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. It is noted that the previous submission of claim amendments does not underline all added text (see claim 12). Applicant is requested to indicate all amendments to the claims in future submissions.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Application/Control Number: 10/052,417

Page 16

Art Unit: 1634

Jehanne Si H

Jehanne Sitton

Primary Examiner

Art Unit 1634

8/18/05